[0014] The antibodies of the present disclosure are useful because they are likely to provide a means of treating the severity and duration of symptoms of a primary infection such as diarrhoea in a patient or preventing death and not just prevent the reoccurrence of disease symptoms.

[0015] In at least some embodiments the antibodies according to the present disclosure show no reduction in potency in the presence of high concentrations of toxin.

DETAILED DESCRIPTION OF THE PRESENT INVENTION

[0016] Specific as employed herein is intended to refer to an antibody that only recognises the antigen to which it is specific or an antibody that has significantly higher binding affinity to the antigen to which is specific compared to binding to antigens to which it is non-specific, for example 5, 6, 7, 8, 9, 10 times higher binding affinity.

[0017] Binding affinity may be measured by standard assays such as surface plasmon resonance, such as BIAcore.

[0018] In one embodiment the EC_{50} is less than 75, 70, 60, 65, 55, 50, 45, 40, 35, 30, 25, 20, 15, 10, 9, 8, 7, 6, 5, 4, 3, 2, 1.5 ng/ml *Clostridium difficile* infection in cell culture assays and the patient. This is significantly lower (more potent) than known antibodies and is thought to be a major factor as to why the antibodies of the present disclosure have a significant and positive impact on survival of subjects receiving treatment.

[0019] As employed herein potency is the ability of the antibody to elicit an appropriate biological response, for example neutralisation of the deleterious toxin effects, at a given dose or concentration. Examples of potency include the percent maximal neutralisation of toxin activity (extent of protection), the lowest relative concentration of Mab to antigen (e.g. EC_{50}), the speed and durability of neutralisation activity.

[0020] In cell culture assays neutralisation might be observed as one or more of the following: prevention of binding of toxin to cells, immunoprecipitation of toxin from solution, prevention of loss of cell form and shape, prevention of loss of cytoskeletal structures, prevention of loss of cell monolayer tight junctions and trans-epithelial electrical resistance, prevention of cell death, apoptosis and production of pro-inflammatory cytokines such as TNFα, IL-1β, IL-6 and MIP1α.

[0021] In tissue section and explant assays neutralisation may, for example be observed as prevention of necrosis and/or oedematous fluid accumulation.

[0022] In in vivo assays neutralisation may be observed as one or more of the following: prevention of fluid accumulation in ligated ileal loops and prevention of gut tissue necrosis, diarrhoea, pseudo-membrane formation of death of animals,

[0023] Thus in one embodiment there is provided an antibody (for example an anti-toxin A antibody) comprising a CDR, such as 1, 2, 3, 4, 5 or 6 CDRs, selected from:

```
                                         SEQ ID NO: 1
QASQSISNALA

                                         SEQ ID NO: 2
SASSLAS

                                         SEQ ID NO: 3
QYTHYSHTSKNP
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-continued
                                         SEQ ID NO: 4
GFTISSYYMS

                                         SEQ ID NO: 5
IISSGGHFTWYANWAKG

                                         SEQ ID NO: 6
AYVSGSSFNGYAL
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[0024] In one embodiment sequences 1 to 3 are in a light chain of the antibody.

[0025] In one embodiment sequences 4 to 6 are in a heavy chain of the antibody.

[0026] In one embodiment SEQ ID NO: 1 is CDR L1, SEQ ID NO: 2 is CDR L2 and SEQ ID NO; 3 is CDR L3.

[0027] In one embodiment SEQ ID NO: 4 is CDR H1, SEQ ID NO: 5 is CDR H2 and SEQ ID NO; 6 is CDR H3.

[0028] In one embodiment SEQ ID NO: 1 is CDR L1, SEQ ID NO: 2 is CDR L2, SEQ ID NO; 3 is CDR L3, SEQ ID NO: 4 is CDR H1, SEQ ID NO: 5 is CDR H2 and SEQ ID NO; 6 is CDR H3.

[0029] In one embodiment there is provided a variable region, such as a light chain variable region with the following sequence (Antibody 922 anti-toxin A antibody; Light chain Variable region sequence) SEQ ID NO: 7:

DPVMTQSPSTLSASVGDRVTITC<u>QASQSISNALA</u>WYQQKPGKAPKLLIY<u>S</u>

<u>ASSLAS</u>GVPSRFKGSGSGTEFTLTISSLQPDDFATYYC<u>QYTHYSHTSKNP</u>

FGGGTKVEIK

wherein the CDRs are underlined and construct is referred to herein as 922.g1 VK (gL1).

[0030] The polynucleotide sequence encoding SEQ ID NO: 7 is shown in FIG. 1 and SEQ ID NO: 8 therein.

[0031] In one embodiment there is provided a variable region, such as a heavy chain variable region with the following sequence (Antibody 922 anti-toxin A antibody heavy chain variable region sequence) SEQ ID NO: 9:

EVQLVESGGGLVQPGGSLRLSCAAS<u>GFTISSYYMS</u>WVRQAPGKGLEWIG<u>I</u>

<u>ISSGGHFTWYANWAKG</u>RFTISSDSTTVYLQMNSLRDEDTATYFCAR<u>AYVS</u>

<u>GSSFNGYAL</u>WGQGTLVTVS

wherein the CDRs are underlined and construct is referred to herein as 922.g1 VH (gH1)

[0032] The polynucleotide sequence encoding SEQ ID NO: 9 is shown in FIG. 1 and SEQ ID NO: 10 therein.

[0033] In one embodiment the antibody comprises the variable regions shown in SEQ ID NO: 7 and 9.

[0034] Thus in one embodiment there is provided an antibody (for example an anti-toxin A antibody) comprising a CDR, such as 1, 2, 3, 4, 5 or 6 CDRs, selected from:

```
                                         SEQ ID NO: 11
QASQSISNYLA

                                         SEQ ID NO: 12
SASTLAS

                                         SEQ ID NO: 13
QYSHYGTGVFGA
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